Systematic Assessment of Adult Patients' Satisfaction with Various Eosinophilic Esophagitis Therapies

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Abstract: BACKGROUND AND AIMS The treatment options for eosinophilic esophagitis (EoE) patients include drugs (proton pump inhibitors [PPIs], swallowed topical corticosteroids [STCs]), elimination diets, and dilation. Given the lack of data, we aimed to assess adult EoE patients' satisfaction with different EoE-specific treatment modalities. PATIENTS AND METHODS We evaluated therapy satisfaction recalled over a 12-month period using the validated Treatment Satisfaction Questionnaire for Medication that assesses effectiveness, side effects, convenience, and overall satisfaction. The score for each scale ranges from 0 (dissatisfied) to 100 (satisfied). To evaluate satisfaction with nonpharmacologic therapies, the questionnaire was modified and debriefed into three focus groups. The final questionnaire was sent to 147 patients. RESULTS The patient response rate was 74%. In the last 12 months, 24, 75, 19, and 9% were treated with PPIs, STCs, elimination diet, and dilation, respectively. Patients identified the following considerations as important for therapy choice: effect on symptoms (89%), effect on esophageal inflammation (76%), side effects (69%), and ease of use (58%). Patients found STCs to be effective (83 points), convenient (83 points), and experienced no side effects when using this therapy. When using STCs alone (43%), overall patient satisfaction was high (86 points). Patients judged PPIs to be most convenient (89 points), STCs to be a bit less convenient (83 points), and diet to be most inconvenient (46 points) of the three therapies examined. CONCLUSIONS Adult EoE patients consider both therapy effect on symptoms and esophageal inflammation as important criteria when choosing EoE therapy and appear to be satisfied with STC use.

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Systematic Assessment of Adult Patients' Satisfaction with Various Eosinophilic Esophagitis Therapies

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Keywords
Eosinophilic esophagitis · Patient satisfaction · Patient governance · Shared decision-making

Abstract
Background and Aims: The treatment options for eosinophilic esophagitis (EoE) patients include drugs (proton pump inhibitors [PPIs], swallowed topical corticosteroids [STCs]), elimination diets, and dilation. Given the lack of data, we aimed to assess adult EoE patients' satisfaction with different EoE-specific treatment modalities. ***Patients and Methods:*** We evaluated therapy satisfaction recalled over a 12-month period using the validated Treatment Satisfaction Questionnaire for Medication that assesses effectiveness, side effects, convenience, and overall satisfaction. The score for each scale ranges from 0 (dissatisfied) to 100 (satisfied). To evaluate satisfaction with nonpharmacologic therapies, the questionnaire was modified and debriefed into three focus groups. The final questionnaire was sent to 147 patients. ***Results:*** The patient response rate was 74%. In the last 12 months, 24, 75, 19, and 9% were treated with PPIs, STCs, elimination diet, and dilation, respectively. Patients identified the following considerations as important for therapy choice: effect on symptoms (89%), effect on esophageal inflammation (76%), side effects (69%), and ease of use (58%). Patients found STCs to be effective (83 points), convenient (83 points), and experienced no side effects when using this therapy. When using STCs alone (43%), overall patient satisfaction was high (86 points). Patients judged PPIs to be most convenient (89 points), STCs to be a bit less convenient (83 points), and diet to be most inconvenient (46 points) of the three therapies examined. ***Conclusions:*** Adult EoE patients consider both therapy effect on symptoms and esophageal inflammation as important criteria when choosing EoE therapy and appear to be satisfied with STC use.

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Introduction

Three types of therapies, namely drugs, diets, and dilation, are used to manage adult patients with eosinophilic esophagitis (EoE) [1, 2]. In EoE, the drug-based therapy with most randomized placebo-controlled trial-generated evidence of efficacy is swallowed topical corticosteroids (STCs) taken in the form of either syrup (budesonide diluted in sucralose solution), powder (obtained from blisters of fluticasone propionate inhaler discus or budesonide capsules), or spray (fluticasone propionate oral aerosol inhaler) [1]. STCs are currently used mostly off-label given that a formulation of budesonide developed specifically for adult EoE patients was only recently approved by the European Medicines Agency (in 2017) and Swiss regulators (in 2018) [3]. Proton pump inhibitors (PPIs) are used in a subset of EoE patients responsive to this medication or else in those suffering from concomitant gastroesophageal reflux disease [1]. Six-food (or less) elimination diet is a non-drug-based alternative for EoE management. Just like STCs, the diet may lead to a reduction in esophageal inflammation and symptom relief [1]. Lastly, dilation of strictures often results in symptom relief that may be long-lasting; however, this measure does not affect the inflammatory activity of the disease [1]. These therapy options are associated with either a risk of side effects, potential long-term sequelae associated with uncontrolled inflammation (dilation), or else need for long-term avoidance of staple foods such as milk, wheat, and eggs (diet). As such, patients' perception of the efficacy and safety as well as lifestyle preferences may profoundly influence the choice of EoE-specific therapy.

To date, adult patients' satisfaction with various EoE-specific therapies has not been systematically assessed. The Treatment Satisfaction Questionnaire for Medication (TSQM) is a validated, general measure of patients' satisfaction with medication [4, 5]. We used the questions of the TSQM as well as those specifically developed for the purposes of this study to perform a questionnaire-based survey. In this prospective survey study, we aimed to evaluate the utilization of various EoE-specific therapies, assess adult patients' satisfaction with the therapies they received in the last 12 months, and examine factors that are important for patients' choice of therapy.

Patients and Methods

An overview of the key steps described in this section is shown in Figure 1.

Study Population

Between September and November 2016, adult EoE patients (≥17 years of age) were recruited in one ambulatory care clinic in Switzerland as part of the Swiss Eosinophilic Esophagitis Cohort Study [6]. Disease diagnosis was established by the investigators according to standardized criteria [1]. Patients with concomitant gastroesophageal reflux disease were also included.

Development of the Preliminary Version of the Study Questionnaire

We first created the questionnaire querying various demographic and disease-specific characteristics, utilization of various EoE-specific therapies, and patients' satisfaction with the therapies used in the last 12 months.

The initial questionnaire contained the following 10 domains: sociodemographic characteristics (8 items), EoE-specific patient history (3 items), presence of gastroesophageal reflux (1 item), presence of atopic diseases (4 items), 5 items on past and present EoE-specific therapy (including PPIs, STCs, systemic corticosteroids, diets, and dilation), and factors that are important for patients' choice of therapy (2 items). In addition, the questionnaire contained validated items (questions) from the TSQM that assesses treatment satisfaction with various therapies [4, 5]. Patients were asked to think of the satisfaction with various therapies when looking back at the 12-months period. The TSQM was previously translated into German and underwent cultural adaption for Switzerland (TSQM version 1). The validated TSQM covers the most relevant aspects of patients' satisfaction with medication. The TSQM consists of 14 items falling into 4 scales: effectiveness (3 items), side effects (5 items), convenience (3 items), and overall satisfaction (3 items) (online suppl. Table 1; for all online suppl. material, see www.karger.com/doi/10.1159/000504846) [4, 5]. Unlike many other similar measures, the TSQM may also be used to compare various patient conditions and medication types. The TSQM scale was used five times in the initial questionnaire (including PPIs, STCs, systemic corticosteroids, diet, and dilation). The TSQM scale scores range from 0 (lack of effectiveness) to 100 (excellent effectiveness).

Focus Groups and Individual Patient Interviews

The focus group and individual patient interviews were conducted in accordance with the ISPOR PRO Good Research Practices Task Force report [7, 8]. The purpose of the focus groups was to aid in the item generation phase of questionnaire development and to ensure that "respondents understand how to complete the questionnaire, how to reference the correct recall period, the meaning of the items, how to use the response scales, and any other questionnaire features that may influence patient responses in the intended mode of administration" [7, 8].

We created semistructured interview guides which contained questions and probing strategies to assess patients' understanding of instructions, stem, response options, and format of individual items. Depending on the item, questions/probing strategies were also used to assess appropriateness of recall period. Lastly, content coverage, format, and length of the entire questionnaire were assessed. A board-certified psychologist from the Division of Psychiatry, University Hospital Basel, conducted two rounds of the cognitive interviews based on these semistructured interview guides. Each focus group lasted approximately 2 h. Two facilitators were also present during the focus groups discussions

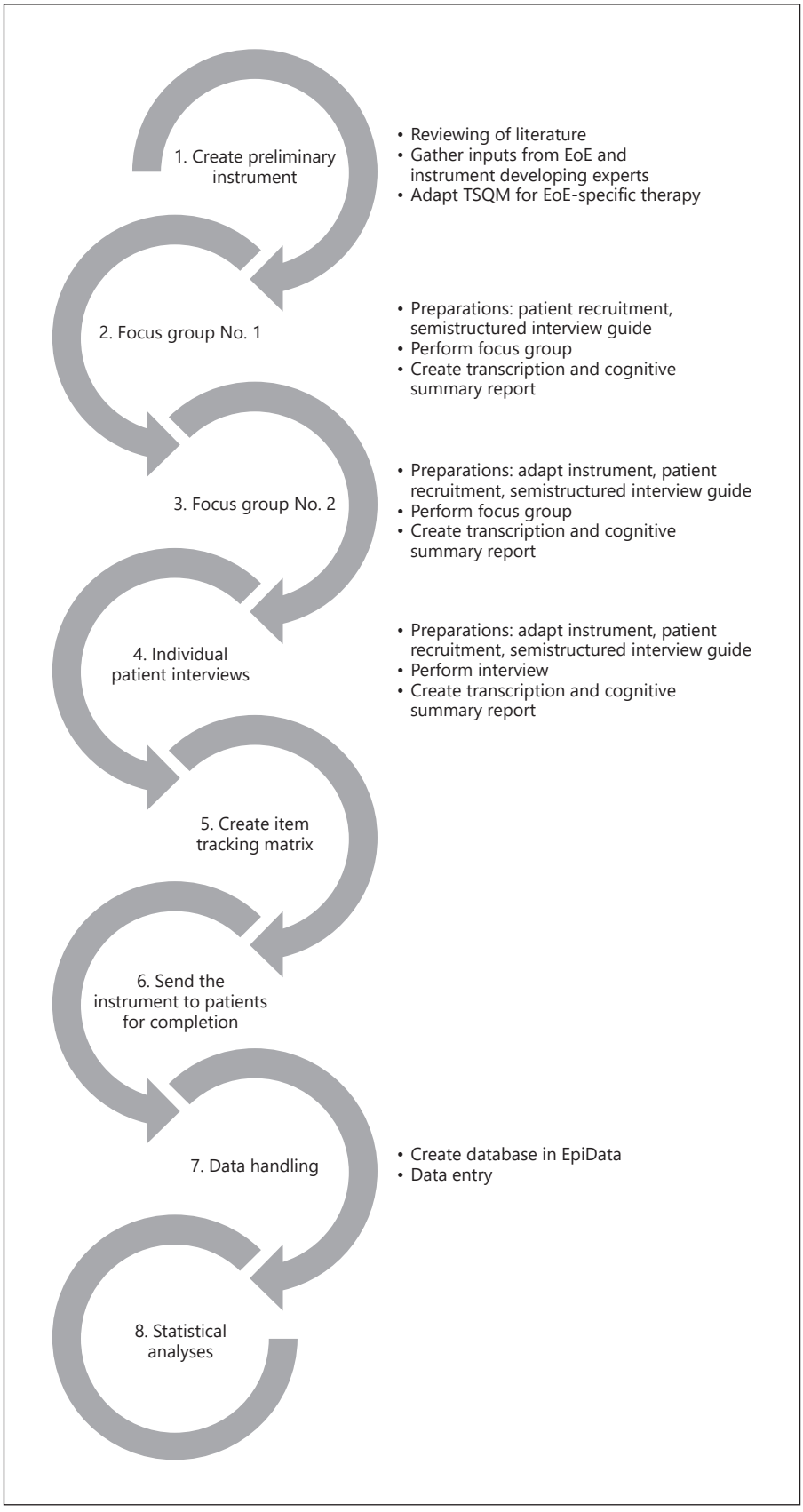

Fig. 1. An overview of the key steps described in Patients and Methods.

Table 1. Characteristics of the respondents

Characteristics (n = 108)	Frequency	%
Age at EoE diagnosis, years	39.0±15.6	NA
Age at inclusion, years	46.9±15.3	NA
Diagnostic delay, years	2.3 (0.3–9.3), 0–38.3	NA
Disease duration, years	7.6±5.1	NA
Symptom severity as assessed by the EEsAI PRO score[1]	12 (0–27), 0–65	NA
EoE-specific quality of life as assessed by the EoE-QoL-A[2]	0.5 (0.29–0.96), 0–1.83	NA
Male sex	85	78.7
Family history of EoE	23	6.5
Nationality		
Swiss	98	90.7
Non-Swiss	10	9.3
ISCED 2011 education level		
Level 3	50	46.3
Level 6 or higher	58	53.7
Experienced food bolus impaction requiring endoscopic disimpaction (ever)	39	36.1
Gastroesophageal reflux disease		
Ever diagnosed	28	25.9
Heartburn in the last 7 days	29	26.9
Concomitant allergies (ever in life)		
Asthma	37	34.3
Allergic rhinitis	64	59.3
Neurodermitis	27	25.0
Known food allergies	42	38.9
More than one condition	54	50.0
EoE-specific therapy		
STCs (budesonide or fluticasone), ever	106	98.1
STCs at inclusion	81	75.0
Elimination diets, ever	27	25.0
Elimination diets at inclusion	20	18.5
Esophageal dilation, ever	38	35.2
Esophageal dilation within the last 12 months	10	9.3
PPI therapy		
Ever	49	45.4
At inclusion	26	24.1

Values are presented as mean ± SD, median (IQR) and range, or *n*. EEsAI PRO, Eosinophilic Esophagitis Activity Index Patient-Reported Outcomes; EoE, eosinophilic esophagitis; EoE-QoL-A, Eosinophilic Esophagitis Quality of Life Questionnaire for Adults; ISCED, International Standard Classification of Education [11]; NA, not applicable; PPI, proton pump inhibitor; STCs, swallowed topical corticosteroids. [1] The EEsAI PRO questionnaire assesses symptom severity in adults with EoE; the score ranges from 0 points (no symptoms) to 100 points (most severe symptoms) (7-day recall period) [9]. [2] The EoE-QoL-A questionnaire measures EoE-specific quality of life; the score ranges from 0 points (perfect quality of life) to 4 points (very bad quality of life) (7-day recall period) [10].

(D.H. and either A.M.S. or A.S.). D.H. conducted four individual face-to-face semistructured interviews to find out whether last changes to the questionnaire had to be made. An individual patient interview lasted approximately 40 min. Focus group/individual patient interviews were recorded, translated from Swiss German (not a written language) into German, and transcribed. The research team reviewed the transcriptions of the focus groups.

Forty-five and 6 EoE patients were approached during a routine clinical visit in the EoE clinic (Olten, Switzerland) and invited to participate in the focus groups and the face-to-face patient interviews, respectively. Thirty-three and 2 patients declined the invitation for the focus group and the face-to-face patient interviews, respectively. Twelve EoE patients were interviewed during two focus groups (n = 6 for each focus group). Of the 6 patients with a mean age of 38.5 years (range 26–51) participating in focus group 1, 2 were female. Of the 6 patients with a mean age of 47.3 years (range 34–63) participating in focus group 2, 1 was female. Four male patients with a mean age of 59.5 years (range 44–86) were interviewed individually.

Table 2. Median TSQM scores and interquartile range

TSQM scales	PPI (n = 27); median treatment duration 6 years (3–9)	STC (n = 83); median treatment duration 5 years (2–6)	Diet (n = 21); median treatment duration 2 years (1–4.5)
Effectiveness	66.7 (38.9–77.8)	83.3 (66.7–100.0)	77.8 (50.0–88.9)
Side effects[1]	100.0 (100.0–100.0)	100.0 (100.0–100.0)	100.0 (100–100.0)
Convenience	88.9 (77.8–100.0)	83.3 (66.7–100.0)	45.8 (33.3–66.7)
Overall satisfaction	71.4 (50.0–85.7)	78.6 (64.3–92.9)	78.6 (50.0–92.9)
Average score	79.9 (70.3–85.5)	84.8 (73.0–93.1)	76.6 (59.8–81.9)

PPI, proton pump inhibitor; STC, swallowed topical corticosteroid; TSQM, Treatment Satisfaction Questionnaire for Medication.
[1] On the side effect scale, a score of 100 is given to patients who do not experience any side effects.

Final Questionnaire

We created a cognitive summary report and an item tracking matrix documenting all the changes that were made, which included the following: (1) a single item assessing the presence of atopic diseases was separated into 5 items; (2) the part about treatment satisfaction with STCs was expanded to include three different forms of application, namely syrup, powder, and spray, as one participant of the focus group took the STC in two different formulations and was satisfied with one form of application, but not with another; and (3) several items querying the use of concomitant therapies were introduced.

The final questionnaire (online suppl. material) consisted of the following 11 domains: sociodemographic characteristics (7 items), EoE-specific patient history (3 items), presence of reflux (1 item), presence of atopic diseases (4 items), concomitant therapies (including antacids, H2 receptor antagonists, PPIs, and corticosteroids, 7 items), 5 items on past and present EoE-specific therapy (including PPIs, STCs, systemic corticosteroids, diets, and dilation), and factors that are important for patients' choice of therapy (2 items). The final questionnaire contained the TSQM, which was used six times for assessment of satisfaction with PPIs, STCs (once per different application form – syrup, powder, and spray), and dilation [4, 5]. The final questionnaire also included the items of the Eosinophilic Esophagitis Activity Index Patient-Reported Outcomes questionnaire and the Eosinophilic Esophagitis Quality of Life Questionnaire for Adults [9, 10].

Changes to the TSQM

The TSQM was developed for pharmacologic treatments and used in its original form for PPIs and STCs. Given the fact that some patients took PPIs and/or STCs for many years, the "I don't remember" response option to item three of the TSQM ("time until the drug started working") was introduced. The TSQM was adapted for diet and dilation, for which not all TSQM items were applicable (for diet, the item on ease of use related to formulation was removed; for dilation, the entire convenience scale was removed). The word "medication" was replaced with either "diet" or "dilation" and a complementary verb.

Data Handling and Statistical Analysis

We double entered the data into the EpiData (version 3.1, Denmark) database, compared our entries, and extracted the data into Stata (version 13, USA). Data were fairly complete as only two missing responses were found for the lead in items that inquired whether the patient had taken STCs in the last 12 months, and no missing values were found for PPIs, diets, or dilation. For all therapy types, no values for any of the TSQM items were missing. Descriptive results are presented as frequencies and percentages of the group total or median, IQR, and range. Multivariable logistic regression modeling was performed to evaluate the potential factors that might be associated with the outcome "assigning most importance to effects of therapy on symptoms and esophageal inflammation as opposed to symptoms alone." The following variables were entered into the model as independent variables: age, female sex, disease duration, history of esophageal dilation, history of endoscopic disimpaction, education level (university education or equivalent [11]), and anti-inflammatory therapy at the time of study participation (either individually or more than one therapy). In a first step, the potential associated factors were tested separately. In a second step, all factors with a p value <0.15 were entered together into the multivariable logistic regression model. To assess the possibility of effect modification, we evaluated pairwise interaction terms of predictor variables. A p value <0.05 was considered statistically significant.

Results

Patient Characteristics

The final version of the questionnaire was sent by mail to 147 adults with EoE. The survey response rate was 74% (108/147). Patient and disease characteristics are shown in Table 1. Mean patient age was 46.9 ± 5.3 years, 85/108 patients (79%) were male, and mean disease duration was 7.6 ± 5.1 years. At inclusion, 45, 75, and 19% were treated with PPIs, STCs, and food elimination diet, respectively. In the past 12 months, 10 patients underwent esophageal dilation. Thirty-five patients (32%) were managed with more than one therapy (28 patients [26%] with more than one anti-inflammatory therapy). Ten patients (9.3%) did not receive any treatment.

Table 3. Median TSQM scores and interquartile ranges for STCs in powder form in patients with that therapy only as well as combined with either PPIs or diets

TSQM scales	STC only (n = 44)	STC + PPI (n = 19)	STC + diet (n = 9)
Effectiveness	83.3 (72.2–100.0)	77.8 (61.1–94.4)	83.3 (72.2–88.9)
Side effects[1]	100.0 (100.0–100.0)	100.0 (87.5–100.0)	100.0 (100.0–100.0)
Convenience	77.8 (66.7–100.0)	83.3 (66.7–100.0)	94.4 (83.3–100.0)
Overall satisfaction	85.7 (64.3–92.9)	85.7 (57.1–96.4)	78.6 (71.4–85.7)

PPI, proton pump inhibitor; STC, swallowed topical corticosteroid; TSQM, Treatment Satisfaction Questionnaire for Medication.
[1] On the side effect scale, a score of 100 is given to patients who do not experience any side effects.

Table 4. Criteria important for the choice of therapy (n = 108)

	Frequency	%
Effect on symptoms	96	88.9
Effect on inflammation in the esophagus	82	75.9
Potential side effects	75	69.4
Ease of use	63	58.3
Treating physician's recommendation	54	50.0
Compatibility with lifestyle	50	46.3
Price	21	19.4
Recommendation of other patients with this condition	12	11.1
One's own research (for example, on the internet)	9	8.3
Needs of the family	5	4.6
Other reasons	5	4.6

Satisfaction with Therapy

The TSQM scale scores as well as the average TSQM values for PPIs, STCs, and diet are shown in Table 2 (patients could be on more than one therapy in the past 12 months). When judging the convenience of using these EoE-specific therapies, patients found PPI use to be most convenient (score of 89). Although most patients needed to extract the steroid powder-containing blister from the discus of asthma-specific medication, they found STCs to be relatively convenient (score of 83). Patients on elimination diet found this therapy to be fairly inconvenient (score of 46). Patients did not observe any side effects associated with the use of various EoE-specific therapies, which is consistent with their long-term use (especially PPIs and STCs, which were used for the duration of 6 and 5 years, respectively).

We also examined therapy satisfaction in the population that used STCs only (in powder form), STCs together with PPIs, and STCs together with elimination diets (Table 3). Patients found STCs to be effective (score of 83), relatively convenient (score of 78), and experienced no side effects when using this therapy. When using STCs alone, overall satisfaction was fairly high (score of 86).

Criteria Important for the Choice of Therapy

The criteria that patients find important for the choice of therapy are shown in Table 4. The effect of therapy on symptoms (89%) and esophageal inflammation (76%), possible side effects (69%), and ease of therapy use (58%) were identified by patients as important considerations for the choice of therapy. When asked about the most important criterion for the choice of therapy (Fig. 2), 45, 32, and 11% of patients chose the effect of treatment on symptoms and esophageal inflammation, the effect of treatment on the symptoms alone, and the effect of treatment on esophageal inflammation alone, respectively, as the deciding factor.

Stepwise logistic regression modeling was performed to identify factors associated with assigning most importance to improvement in symptoms and inflammation compared to that in symptoms alone as criteria for the choice of therapy (Table 5). In the univariable model, female sex, STC use, and PPI use at the time of the study were positively associated with putting greater emphasis on improvement in symptoms and esophageal inflammation compared to that in symptoms alone, whereas presence of at least a university degree (or equivalent) was negatively associated with this outcome. In the multivariable analysis, female sex (OR 3.727, 95% CI 0.996–13.944, p = 0.050), STC use at the time of the study (OR 3.760, 95% CI 1.125–12.565, p = 0.031), and PPI use at the time of the study (OR 2.911, 95% CI 0.869–9.754, p = 0.083) were positively associated with outcome. In the multi-

Table 5. Uni- and multivariable logistic regression evaluating factors associated with assigning most importance to control of inflammation and symptoms ($n = 49$) over control of symptoms alone ($n = 34$)

	Univariable			Multivariable		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age, years	0.996	0.967–1.025	0.793			
Female sex	3.636	1.093–12.098	0.035	3.727	0.996–13.944	0.050
Disease duration (diagnosed), years	1.042	0.949–1.144	0.389			
Dilation (ever)	0.922	0.360–2.363	0.866			
Disimpaction (ever)	0.809	0.319–2.049	0.655			
Education level (ISCED level ≤3 vs. ≥6)	0.390	0.156–0.971	0.043	0.406	0.148–1.117	0.081
STC use at the time of the study	2.451	0.863–6.963	0.092	3.760	1.125–12.565	0.031
PPI use at the time of the study	2.320	0.747–7.207	0.146	2.911	0.869–9.754	0.083
Elimination diet at the time of the study	0.989	0.335–2.922	0.984			

ISCED, International Standard Classification of Education; PPI, proton pump inhibitor; STC, swallowed topical corticosteroid.

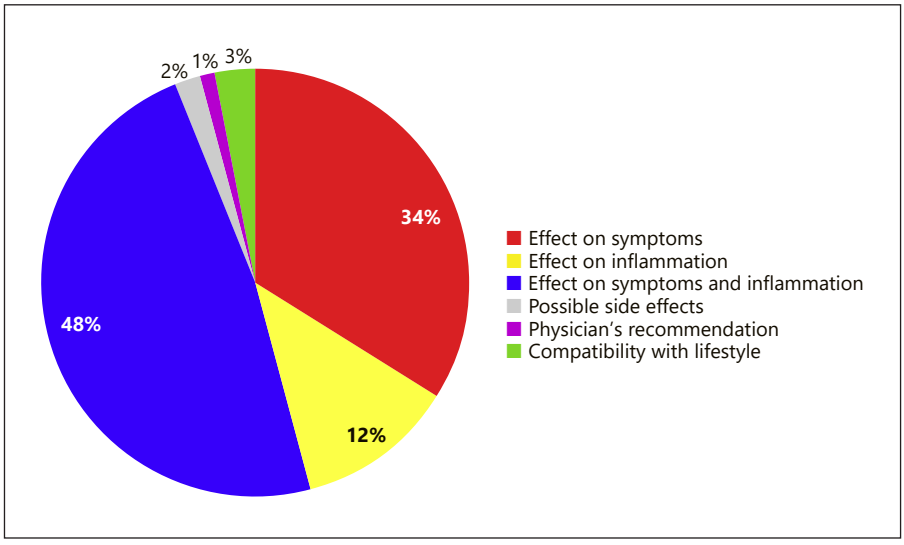

Fig. 2. The most important criteria for the choice of therapy. EoE, eosinophilic esophagitis; TSQM, Treatment Satisfaction Questionnaire for Medication.

variable analysis, we observed a trend for negative association between presence of at least a university degree (or equivalent) and outcome (OR 0.406, 95% CI 0.148–1.117, $p = 0.081$). We also carried out regression modeling, in which the use of more than one anti-inflammatory therapy at the time of the study (as opposed to each therapy individually) was examined. We found that use of more than one anti-inflammatory therapy was positively associated with putting greater emphasis on improvement in symptoms and esophageal inflammation compared to that in symptoms alone in both univariable (OR 6.544, 95% CI 1.753–24.427, $p = 0.005$) and multivariable analyses (OR 9.294, 95% CI 2.309–37.405, $p = 0.002$ for more than one anti-inflammatory therapy; OR 3.874, 95% CI 1.061–14.152, $p = 0.040$ for female sex; OR 0.385, 95% CI 0.137–1.080, $p = 0.070$ for presence of at least a university degree).

Discussion

This is the first study examining adult EoE patients' satisfaction with different therapies using a validated questionnaire. We developed a survey to assess treatment satisfaction with EoE-specific therapy by consulting the ISPOR guidelines and the literature describing the use of the TSQM as well as obtaining input from EoE patients by the means of focus groups and individual interviews.

Patients with a long-established EoE diagnosis appear to be satisfied with anti-inflammatory therapies, especially STCs. We also found that the effects of therapy on symptoms and esophageal inflammation were important considerations for the choice of therapy in adults with EoE, and that female patients and those using anti-inflammatory therapies at the time of the study were more likely to assign greater importance to the effect of therapy on both inflammation and symptoms as opposed to symptoms alone.

With an average TSQM score of 80, 85, and 77 for PPIs, STCs, and diet, respectively, EoE patients appeared to be satisfied with these EoE-specific therapies. The overall satisfaction scores as well as the various TSQM scale scores were consistent with our current knowledge about these therapies. It is well known that whilst STCs and diets appear to be efficacious/effective in the entire EoE patient population, PPIs are only effective in a subset of EoE [12]. Hence, the effectiveness scores are higher for both STCs and diet when compared to PPIs. Although high side effect scale scores are indicative of lack of therapy-related side effects, it is more likely that these patients had been diagnosed with EoE for a relatively long time and would have had time to switch therapy in case of side effects. It is also not surprising that PPIs that are administered in tablet form received the highest convenience score when compared to STC blisters that need to be extracted from the fluticasone discus inhaler developed for asthma patients and diets adhering to which require patients to cook their own meals. Given that many of the patients take the pharmacologic therapies for an extended period of time (median treatment duration of ≥5 years), it is only fitting that overall relatively high satisfaction scores are observed, as both PPIs, STCs, and diets have proven efficacy/effectiveness in patients with esophageal eosinophilia [12–14]. The overall satisfaction scores might have been different (and potentially lower) if therapy satisfaction had been evaluated in newly diagnosed patients needing to decide on the type of therapy that would work best for them and encountering side effects of these therapies.

When asked about considerations that are important for therapy choice, adult EoE patients consider the effect of medication on both symptoms and esophageal inflammation as important. The finding that from the patients' perspective therapy should target both inflammation and symptoms is consistent with the choice of endpoints for most recent trials testing the short-term efficacy of STCs in adults with EoE for the purposes of regulatory approval [15]. We found that female patients and those using single anti-inflammatory therapy or a combination of those therapies at the time of the study were more likely to assign importance to the effect of therapy on both symptoms and esophageal inflammation as opposed to symptoms alone. Given that the majority of patients received a maintenance therapy of 0.25 mg of STC b.i.d., a dose that brings only 16% of all patients into complete remission, it is likely that disease activity in some of these patients on combination therapy was not adequately controlled [16, 17].

According to Atkinson et al. [4], therapy satisfaction is a subset of overall patient satisfaction. Besides therapy satisfaction, overall patient satisfaction covers all other "aspects of medical treatments, interpersonal aspects of clinical care, and processes of treatment" [4]. Overall patient satisfaction interacts with the behavior of patients as well as with decision-making. This relationship between overall patient satisfaction and patient's behavior is not considered to be strictly causal in nature, but rather an interaction between the domains that can influence each other. For example, overall patient satisfaction (and therapy satisfaction) can influence patients' behavior. We hypothesize that when an EoE patient is satisfied with STC therapy (e.g., because of relative ease of use, effectiveness, or few side effects), it is more likely that this patient will pursue the treatment in the long run, even though most EoE symptoms will be gone following a short induction treatment. Given that EoE is a chronic disease, it is important for patients to adhere to anti-inflammatory treatment, as patients with adequate disease control have fewer long-term complications such as food bolus impactions [18]. It is also possible for patients' behavior to influence therapy satisfaction. We hypothesize that an EoE patient who is well informed about the advantages (e.g., no need for medication) and disadvantages (e.g., may lead to lifestyle alterations) of dietary therapy for disease management is more likely to continue the therapy. As such, one could argue that minimizing the rates of therapy discontinuation through, among other things, better patient education might lead to a higher degree of satisfaction with EoE-specific therapy.

The results of this study should be interpreted with several considerations in mind. Although this is the first study attempting to assess patients' satisfaction with various EoE-specific therapies, patients with a long-established diagnosis from one gastroenterology practice specialized in the management of this condition were recruited. It is likely that the high rates of therapy satisfaction might be a consequence of the following: (1) we

ended up with a population of patients that used the therapies for a long time; and (2) it is likely that at least a proportion of patients, especially those participating in various clinical studies, were well informed about the various aspects of this disease. As such, our results may not be generalizable to newly diagnosed patients or those attending less specialized gastroenterology practices. Whilst patients' satisfaction with PPIs and STCs could be evaluated using the original form of the questionnaire, the questionnaire had to be adapted for diet and dilation. Although minor word changes were performed or else nonapplicable items were removed entirely, satisfaction with diet was queried using a unvalidated form of this questionnaire, and the data obtained should be interpreted with caution. Although we used a validated TSQM, it is important to point out that the validity of the overall questionnaire was not rigorously assessed. This is especially true for the items querying the importance of the effects of therapy on various aspects of the disease, as these were not evaluated against another valid questionnaire or construct. The rate of dietary treatment observed in this study was lower (19%) than that observed in centers specialized in elimination diets (up to 57% in a mixed adult and pediatric population) [19]. However, it is important to point out that removal of inflammation-causing foods, such as milk- and wheat-based products, might pose challenges as these foods represent important dietary staples of Swiss German patients. Therefore, it is likely that, among other things, Swiss German patients' dietary and physicians' personal preferences contributed to high rates of STC use in the current population.

In conclusion, we found that patients with a long-established EoE diagnosis appear to be satisfied with anti-inflammatory therapies, especially STCs, and consider both symptoms and esophageal inflammation as important targets for therapy.

Statement of Ethics

The study was approved by the ethics committee of the canton Vaud (CER-VD, protocol number 148/15) [6]. Patients provided written informed consent for participation in the study.

Disclosure Statement

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Author Contributions

Study concept and design: 1; acquisition of data: 2; analysis and interpretation of data: 3; drafting of the manuscript: 4; critical revision of the manuscript for important intellectual content: 5; statistical analysis: 6; obtained funding: 7; administrative, technical, or material support: 8; study supervision: 9; guarantor of the article: 10. E. Safroneeva: 1, 2, 3, 4, 5, 6, 8; D. Hafner: 2, 3, 5, 8; C.E. Kuehni: 1, 2, 3, 5, 8; M. Zwahlen: 1, 2, 3, 5, 8; S. Trelle: 2, 3, 5, 8; L. Biedermann: 1, 2, 3, 5, 8; T. Greuter: 1, 2, 3, 5, 8; S.R. Vavricka: 1, 2, 3, 5, 8; A. Straumann: 1, 2, 3, 5, 8; A.M. Schoepfer: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10.

References

1 Lucendo AJ, Molina-Infante J, Arias Á, von Arnim U, Bredenoord AJ, Bussmann C, et al. Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. United European Gastroenterol J. 2017 Apr;5(3):335–58.

2 Schoepfer A, Safroneeva E, Straumann A. Eosinophilic Esophagitis: Impact of Latest Insights Into Pathophysiology on Therapeutic Strategies. Dig Dis. 2016;34(5):462–8.

3 European Medicines Agency. Jorveza. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/004655/human_med_002212.jsp&mid=WC0b01ac058001d124 (last accessed August 6, 2018).

4 Atkinson MJ, Sinha A, Hass SL, Colman SS, Kumar RN, Brod M, et al. Validation of a general measure of treatment satisfaction, the Treatment Satisfaction Questionnaire for Medication (TSQM), using a national panel study of chronic disease. Health Qual Life Outcomes. 2004 Feb;2(1):12.

5 Atkinson MJ, Kumar R, Cappelleri JC, Hass SL. Hierarchical construct validity of the treatment satisfaction questionnaire for medication (TSQM version II) among outpatient pharmacy consumers. Value Health. 2005 Nov–Dec;8(Suppl 1):S9–24.

6 Safroneeva E, Saner C, Rossel JB, Golay D, Pittet V, Godat S, et al.; Swiss EoE Cohort Study Group. Cohort Profile: The Swiss Eosinophilic Esophagitis Cohort Study (SEECS). Inflamm Intest Dis. 2018 Mar;2(3):163–70.

7 Patrick DL, Burke LB, Gwaltney CJ, Leidy NK, Martin ML, Molsen E, et al. Content validity – establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO Good Research Practices Task Force report: part 1 – eliciting concepts for a new PRO instrument. Value Health. 2011 Dec;14(8):967–77.
8 Patrick DL, Burke LB, Gwaltney CJ, Leidy NK, Martin ML, Molsen E, et al. Content validity – establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO Good Research Practices Task Force report: part 2 – assessing respondent understanding. Value Health. 2011 Dec;14(8):978–88.
9 Schoepfer AM, Straumann A, Panczak R, Coslovsky M, Kuehni CE, Maurer E, et al.; International Eosinophilic Esophagitis Activity Index Study Group. Development and validation of a symptom-based activity index for adults with eosinophilic esophagitis. Gastroenterology. 2014 Dec;147(6):1255–66.e21.
10 Taft TH, Kern E, Kwiatek MA, Hirano I, Gonsalves N, Keefer L. The Adult Eosinophilic Oesophagitis Quality of Life questionnaire: a new measure of health-related quality of life. Aliment Pharmacol Ther. 2011 Oct;34(7):790–8.
11 UNESCO. International Standard Classification of Education (ISCED). http://uis.unesco.org/en/topic/international-standard-classification-education-isced (last accessed August 6, 2019).
12 Lucendo AJ, Arias Á, Molina-Infante J. Efficacy of Proton Pump Inhibitor Drugs for Inducing Clinical and Histologic Remission in Patients With Symptomatic Esophageal Eosinophilia: A Systematic Review and Meta-Analysis. Clin Gastroenterol Hepatol. 2016 Jan;14(1):13–22.e1.
13 Arias A, González-Cervera J, Tenias JM, Lucendo AJ. Efficacy of dietary interventions for inducing histologic remission in patients with eosinophilic esophagitis: a systematic review and meta-analysis. Gastroenterology. 2014 Jun;146(7):1639–48.
14 Cotton CC, Eluri S, Wolf WA, Dellon ES. Six-Food Elimination Diet and Topical Steroids are Effective for Eosinophilic Esophagitis: A Meta-Regression. Dig Dis Sci. 2017 Sep;62(9):2408–20.
15 Dellon ES, Katzka DA, Collins MH, Hamdani M, Gupta SK, Hirano I, et al.; MP-101-06 Investigators. Budesonide Oral Suspension Improves Symptomatic, Endoscopic, and Histologic Parameters Compared With Placebo in Patients With Eosinophilic Esophagitis. Gastroenterology. 2017 Mar;152(4):776–786.e5.
16 Greuter T, Bussmann C, Safroneeva E, Schoepfer AM, Biedermann L, Vavricka SR, et al. Long-Term Treatment of Eosinophilic Esophagitis With Swallowed Topical Corticosteroids: Development and Evaluation of a Therapeutic Concept. Am J Gastroenterol. 2017 Oct;112(10):1527–35.
17 Greuter T, Safroneeva E, Bussmann C, Biedermann L, Vavricka SR, Katzka DA, et al. Maintenance Treatment Of Eosinophilic Esophagitis With Swallowed Topical Steroids Alters Disease Course Over A 5-Year Follow-up Period In Adult Patients. Clin Gastroenterol Hepatol. 2019 Feb;17(3):419–428.e6.
18 Kuchen T, Straumann A, Safroneeva E, Romero Y, Bussmann C, Vavricka S, et al. Swallowed topical corticosteroids reduce the risk for long-lasting bolus impactions in eosinophilic esophagitis. Allergy. 2014 Sep;69(9):1248–54.
19 Molina-Infante J, Arias Á, Alcedo J, Garcia-Romero R, Casabona-Frances S, Prieto-Garcia A, et al. Step-up empiric elimination diet for pediatric and adult eosinophilic esophagitis: The 2-4-6 study. J Allergy Clin Immunol. 2018 Apr;141(4):1365–72.